DETAILED ACTION

Response to Amendment

The response and amendment filed on Sept. 19, 2008 have been acknowledged. Claims 1 and 6 have been amended. Claims 2, 4-5, 7-8, 10-19, 21, 23, 25, 29-30, 32-34 and 38-120 have been canceled. Clams 1, 3, 6, 9, 20, 22, 24-28, 31, 35-37, 121-123 are pending. Claims 20, 22, 24, 26-28, 35-37 were withdrawn from consideration. Claims 1, 3, 6, 9, 37, 121-123 within the elected scope of B18R gene as the first mutated gene and an interferon (INF) modulation polypeptide gene as the second mutation are considered before the examiner.

Withdrawn Claim Rejections - 35 USC § 102

1. The rejection of claims 1, 3, 6, 9, 37 under 35 U.S.C. 102(b) as being anticipated by Blanchard et al. (A) (J. Gene. Virol. 1998, Vol. 79, pp. 1159-1167) or in Blanchard et al. (B) (aidsline C13 1997) or Spehner et al. (Virology 2000, Vol. 273, pp. 9-15) light of the teaching by Alcam et al. (J. Gene. Virol. March 2002, Vol. 83, pp. 545-549) has been withdrawn necessitated by Applicant's amendment and the persuasive argument in that note of the cited references teach using Copenhagen or Western Reserve strain of Vaccinia virus as claims amended.

2. The rejection of claims 13, 6, 9, 37 under 35 U.S.C. 102(a) as being anticipated by as being anticipated by Feng t al. (Immunology and Cell Biology Dec. 2001, Vol. 79, pp. 569-575) or Trevor et al. (Cancer Immuno Immunother. Oct. 2001, Vol. 50, pp. 397-407) light of the teaching by Blanchard et al. (A) (J. Gene. Virol. 1998, Vol. 79, pp. 1159-1167) has been removed necessitated by Applicant's amendment and a persuasive argument stated above.

3. The rejection of claims 1, 6, 9, 37, 121 under 35 U.S.C. 102(b) as being anticipated by Roberts et al. (WO 00/62735A2) in light of the teaching by Xiang et al. (J. Virol. May 2002, Vol. 76, No. 10, pp. 5251-5259) has been withdrawn necessitated by Applicants' amendment and the persuasive argument cited above.

Withdrawn Claim Rejections - 35 USC § 103

4. The rejections of claims 1, 3, 6, 9, 37, 121-123 under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Blanchard et al. (A) (J. Gene. Virol. 1998, Vol. 79, pp. 1159-1167) and McCart et al. (Cancer Research Dec. 2001, pp. 8751-8757) or as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Blanchard et al. (A) (J. Gene. Virol. 1998, Vol. 79, pp. 1159-1167) and Roberts et al. (WO

00/62735A2) and Puhlmann et al. (Cancer Gene Therapy 2000, Vol. 7, No. 1, pp. 66-73) has been withdrawn necessitated by Applicant's amendment and the persuasive argument. Because as Applicant asserted that none of the cited references teach using Copenhagen or Western Reserve strain of Vaccinia virus. Applicant further points out that Blanchard et al. teach other vaccinia virus having mutations of B18R and/or B8R is unable to replicate well in mammalian cells. Applicant found that it is an unexpected result that Copenhagen virus and WR virus with such mutation are still able to replicate well.

Claim Rejections - 35 USC § 112 Maintained

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. The rejection of claims 121-123 under 35 U.S.C. 112, first paragraph for the new matter and lacking of writen description is still maintained.

7. Applicant submits that the specification on page 26, line 33 has mentioned about TK gene mutation of vaccinia virus known prior to the current Application was filed. On page 18, the specification also cites "It is specially contemplated that any embodiment discussed with respect to a particular methods of composition of the invention". Because of these, Applicant is entitled to have a supportive description of the claimed invention cited in claims 121-123.

8. Applicant's argument has been respectfully considered; however, it is not found persuasive. First of all, the statement n page 18 was not as related to TK deletion. It is referred to the method using a mutated vaccinia virus alone or in combination with chemotherapy or radiotherapy, wherein the mutation of the attenuated vaccinia virus has not described to contain TK mutation. The specification has described many embodiments of a vaccinia virus mutation; however, TK gene (J2R) mutation is not described as one choice among so many listed mutations on pages 8-17.

9. Moreover, the citation of "thymidine kinase-deletion mutant of vaccinia virus that can infect tumor masses and ovarian tissue taught by Gnant et al" is not cited as a product or method incorporated by reference. More importantly, the reference by Gnant et al. only teach to insert a

marker gene downstream of TK gene, it does not teach to delete or inactive or make a point mutation of TK gene in a vaccinia virus as claims 122-121-123 require.

10. It is well known that the TK gene of different vaccinia viruses vary in length and molecular sequence structure. For example, Copenhagen strain of a vaccinia virus has 177 amino acids. If every amino acid residue had a point mutation and was substituted with other 19 amino acids available in the art, it would give astronomic numbers of mutated TK variants. The specification lacks of teaching any thing related to make the TK gene mutation or inactivation as it was originally filed.

11. Therefore, the new claims 121-123 introduce a new mater into the Application. Applicant is not considered to have a possession for the claimed vaccinia virus cited in claims 121-123.

Double Patenting Maintained

12. Claims 1, 3, 6, 9, 37 are still provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 2, 3, 4, 5, 6, 7, 9 and 37 of copending Application No. 11,838,757.

13. Applicants do not object the rejection and indicate to hold the rejection in abeyance until the present Application has been allowed.

14. Therefore, the pending claims 1, 3, 6, 9 and 37 are still rejected and not in condition for allowance.

New ground of rejection:

Claim Rejections - 35 USC § 102

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

16. Claims 1, 3, 37 are rejected under 35 U.S.C. 102(b) as being anticipated by Alcam et al. (J. Virol. Dec. 2000. Vol. 74, No. 23, pp. 11230-11239) or Symons et al. (Cell 1995, Vol. 81, pp. 551-560).

17. Alcam et al. and Symons et al. all describe a Western reserve strain of vaccinia virus (VVA WR) comprising a deletion mutation in B18R gene (vΔB18R). Therefore, claims 1, 3 and 37 are anticipated by the cited references.

Claim Rejections - 35 USC § 102

18. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

19. Claims 1, 6, 9, 37 and 121, 123 are rejected under 35 U.S.C. 102(b) as being anticipated by Paoletti et al. (US Patent No. 5,762,938) in light of the disclosure by Legrand et al. (PNAS Feb, 2002, Vol. 102, No. 8, pp. 2941-2945).

20. Paoletti et al. describe a method for making a recombinant vaccinia virus vector using Copenhagen strain. Pallotetti et al. teach that the recombinant virus comprises several deleted regions from C23-F4L, C7-K1L, J2R, A26L, A56, I4L and B13R-B29R. The J2R encoding the thymidine kinase gene (TK). Paoletti et al. teach that the TK gene can be completely deleted or inactivated in any way because vaccinia virus with TK gene deletion (TK^-) is still capable of replication in vivo at the site of inoculation in a variety of host by a variety routs. The deletion of B13R-B29R inherently comprises the deletion of B18R. Both B13R and B22R encode factors that modulate the INF expression in light of disclosure by Legrand et al. (PNAS Feb, 2002, Vol. 102, No. 8, pp. 2941-2945). The mutated Copenhagen virus alone with other vaccinia viruses are all prepared as a pharmaceutical composition and tested in vitro or in vivo by Paoletti et al. (Please see claims 4 and 8, Fig. 39, columns 3, 134, 225 and all examples using NYVAC, i.e. Copenhagen strain of vaccinia virus). Therefore, Paoletti et al. anticipate claims 1, 6, 9, 37, 121 and 123.

Claim Rejections - 35 USC § 103

21. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are

such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

22. Claims 1, 3, 6, 9, 37, 37, 121, 123 are rejected under 35 U.S.C. 103(a) as being unpatentable over Claims 1, 6, 9, 37, 121, 123 by Paoletti et al. (US Patent No. 5,762,938) in view of Veradi et al. (J. Virol. 2001, Vol. 75, No. 1, pp. 11-18) for claim 3.

23. Paoletti et al. describe a method for making a recombinant vaccinia virus vector including Copenhagen strain. Paoletti et al. teach that the recombinant virus comprises several deleted regions from C23-F4L, C7-K1L, J2R, A26L, A56, I4L and B13R-B29R. The J2R encoding the claimed thymidine kinase gene (TK). Paoletti et al. teach that the TK gene can be completely deleted or inactivated in any way because vaccinia virus with TK gene deletion (TK^-) is still capable of replication in vivo at the site of inoculation in a variety of host by a variety routs. The deletion of B13R-B29R inherently comprises the deletion of B18R. Both B13R and B22R encode factors that modulate the INF expression in light of disclosure by Legrand et al. (PNAS Feb, 2002, Vol. 102, No. 8, pp. 2941-2945). All of these mutated vaccinia viruses are prepared as a pharmaceutical composition and tested in vitro or in vivo by Paoletti et al. (Please see claims 4 and 8, Fig. 39, columns 3, 134, 225 and all examples using NYVAC, i.e. Copenhagen strain of vaccinia virus). Paoletti et al. do not teach making a mutated vaccinia virus with a B8R gene mutation.

24. Verardi et al. teach a method for making B8R gene deletion from a vaccinia virus, western reserve strain (WR). B8R gene encodes a secreted protein with homology to the gamma interferon (INF-λ) receptor. Verardi et al. demonstrate and concluded that the deletion of the B8R gene had no detectable effects on humoral immune response, and leads to an enhanced safety without a concomitant reduction in immunogenecity.

25. Therefore, it would have been obvious to one ordinarily skilled in the art at the time of the invention was filled to be motivated by the recited references combining the teachings by Paoletti et al. and Verardi et al. to construct a recombinant Copenhagen or Western reserve vaccinia virus with B18R, B8 and TK gene deletions, hereby ensuring the use of the truncated Copenhagen or WR strain more safely.

26. As there are no unexpected results have been provided, the claimed invention as a whole is prima facie obvious absence unexpected results.

Conclusion

No claims are allowed.

27. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BAO LI whose telephone number is (571)272-0904. The examiner can normally be reached on 6:30 am to 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Bao Qun Li/ Examiner, Art Unit 1648

/Bruce Campell/

Supervisory Patent Examiner, Art Unit 1648